REMARKS

Acknowledgment of Applicant's claim of foreign priority to United Kingdom Application No. 0219511.3 is appreciated. The specification has been amended to effect editorial changes to the claim of priority. Also, as requested, a certified copy of United Kingdom Application No. 0219511.3 is attached. The specification has also been amended to include a space between the words "uniformity" and "is" in line 2 of paragraph [0018].

Claims 1-15 have been amended to effect certain editorial changes, most of which were suggested by the Patent office. Claim 6 has been amended to eliminate any improper multiple dependencies.

No new matter has been added.

Turning now to the prior art rejections, claims 1-15 have been rejected under 35 U.S.C. § 103(a) over U.S. Patent 6,030,604 (*Trofast*); claims 1-12 have been rejected under 35 U.S.C. § 103(a) over U.S. Patent 6,284,287 (*Sarlikiotis*); and claims 13-15 have been rejected under 35 U.S.C. § 103(a) over *Sarlikiotis* in view of U.S. Publication 2002/0103260 (*Clarke*). For the following reasons, the rejections are respectfully traversed.

§ 103(a) rejections over *Trofast* and *Sarlikiotis*

A *prima facie* case of obviousness has not been established. Neither cited reference suggests the claimed invention because there is no motivation to modify any of the cited prior art to produce the claimed invention.

Trofast discloses a method of preparing a dry powder composition for treating respiratory disorders. In *Trofast*, one or more pharmaceutically active substances is mixed with a carrier substance, micronized, and treated to further shape them. Thereafter, optionally, another pharmaceutically active

substance may be added to the mixture, and the mixture may be re-micronized.

Sarlikiotis discloses mixing one or more active compounds with an excipient to coat the excipient to produce a pharmaceutical formulation for administration by inhalation.

The Patent office has acknowledged that the claimed invention differs from the teachings of the cited prior art in no fewer than three respects, namely, "the same order of mixing ingredients," "the step of adding a second portion of a first medicament," and the recitation of having different medicaments in different amounts mixed in a specified order based on their relative amounts.

Nonetheless, on pages 4, 5, 7 and 8, the Patent office has still taken the position that despite these three deficiencies, the present invention would have been obvious over *Trofast* or *Sarlikiotis*. Specifically, the Patent office has asserted:

> …it would have been apparent to a skilled artisan that one could add additional active agent as needed. Furthermore, it is noted that the step of mixing components in a method of making a pharmaceutical dry powder is conventionally practiced in the art. It is obvious that the order of mixing ingredients in a composition and the relative amount of ingredients in a composition are clearly result specific parameters. The amount of a specific ingredient in a composition and the order of steps in a process are clearly result effective parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed and the optimal order of combining said ingredients to achieve the desired results.

This reasoning, however, does not constitute a legally acceptable basis for determining obviousness.

According to the M.P.E.P., the "fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness." (M.P.E.P. § 2143.01.IV.) Therefore, the mere possibility that one could add an additional active agent and that the technique of mixing is known do not render the present invention obvious.

It is well established that even though a prior art process or device could be modified so as to produce the claimed invention, there is no basis for an obviousness rejection unless the prior art *suggests* the desirability of such modification. *In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984). As stated in *In re Oetiker*, 997 F.2d 1443, 1447, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992):

> There must be some reason, suggestion, or motivation found *in the prior art* whereby a person of ordinary skill in the field of the invention would make the combination. That knowledge cannot come from the applicant's invention itself. (emphasis added).

Thus, the Patent office alleges that the motivation to produce the claimed invention exists solely by virtue of the optimization of result-effective parameters. However, this assertion is faulty for a number of reasons.

First, M.P.E.P. 2144.05 mandates:

> A particular parameter must be recognized as a result-effective variable, *i.e.*, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 U.S.P.Q. 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor areas

> of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.)

Like the situation in *In re Antonie*, the Patent office has not shown that the cited parameters are result-effective parameters. Specifically, the Patent office has not established that the cited parameters were known to affect uniformity and homogeneity of distribution and separation of the medicament particles from the carriers. Although *Trofast* and *Sarlikiost* disclose the use of mixing, there is no teaching in either reference that the combination of uniformity of distribution and good separation is a function of the order of mixing, the addition of more first medicament, or the relative amounts of the two active agents. *Trofast* and *Sarlikiost* deal with the shape and size of the particles, as evidenced by their focus on micronization and spheronization techniques. Therefore, due to the absence of any disclosure in the cited art of the functionality of the cited parameters, it cannot be said that the present invention is the mere result of routine experimentation of the recited parameters.

Second, resort to the practice of "optimization" to bridge the gap between the prior art and the claimed invention cannot support a finding of obviousness. *Ex parte Stern*, 13 U.S.P.Q.2d 1379, 1381 (BdPatApp&Int 1987). In *Stern*, the Examiner acknowledged that the prior art did not disclose a recited feature relating to high purity levels, but she deemed the feature obvious. *Id.* at 1381. Specifically, the examiner asserted: "Although the prior art fails to recite a protein having such a high specific activity, such is *deemed* obvious relative to the advances in technology that evolves [*sic*, evolve] more sophisticated purification processes that produces

[*sic*, produce] such high degree of purity." *Id.* at 1381. In reversing the obviousness rejection, the Board of Patent Appeals not only found this argument unconvincing, but went so far as to admonish the Examiner: "The Examiner should be aware that 'deeming' does not discharge him from the burden of providing the requisite factual basis and establishing the requisite motivation to support a conclusion of obviousness." *Id.* at 1381.

In the present case, therefore, the assertions that "it would have been apparent to a skilled artisan that one could add additional active agent as needed" and that mixing components and optimization techniques are conventionally practiced in the art cannot support a conclusion of obviousness. No factual basis or motivation in the art has been established. Therefore, the Patent office has not met its burden of establishing a *prima facie* case of obviousness.

Aside from the foregoing, there is no mention in the Official Action that Example 6 of *Sarlikiost* discloses that the first particulate is present in a lower amount than the second particulate. In the claimed method, on the other hand, a portion of a first particulate is mixed with a carrier to produce a first mixture, and then, the second particulate, *which is present in an amount by weight less than the amount by weight of the first particulate*, is mixed with the first mixture. Here, it appears that the Patent office did not consider the teachings of *Sarlikiost* as a whole, but picked and chose specific portions of the reference to support the obviousness rejection. It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art."). *In re Mercer* 515, F.2d 1161, 1165-66, 185 U.S.P.Q. 774, 778 (C.C.P.A. 1975).

Further, neither *Trofast* or *Sarlikiost* teaches the feature recited in claim 4, that the first portion of the first particulate inhalant medicament is in an amount sufficient to create a *monolayer of the first particulate inhalant medicament on the carrier* when they are mixed together. As explained in paragraph [0017] of the present specification, "a key aspect of the invention contributing to the uniformity of disposition, reliability and dose uniformity is that the first portion of the first medicament when mixed with the carrier creates a monolayer on the carrier."

For all of the foregoing reasons, the § 103(a) rejections over *Trofast* and *Sarlikiost* cannot be maintained. Withdrawal of the rejections is respectfully requested.

§ 103(a) rejection over *Sarlikiotis* in view of *Clarke*

Claims 13-15, which ultimately depend from claim 11, have been rejected as obvious over *Sarlikiost* in view of *Clarke*. Specifically, on page 8 of the Official Action, the Patent office asserted:

> Sarlikiotis lacks the teaching of a composition comprising formoterol fumarate dehydrate, a MDPI containing the compositions of the instant invention, and a method of administration comprising inhaling a pharmaceutical composition from a MDPI.
>
> Clarke teaches a pharmaceutical composition comprising (A) **formoterol or a pharmaceutically acceptable salt thereof or a solvate of formoterol or said salt** and (B) fluticasone propionate, suitable for use in the treatment of inflammatory or obstructive airways diseases (abstract).

On page 9, as with the foregoing obviousness rejections, the Patent office also added:

> Although Sarlikiost does not expressly teach the step of adding a second portion of a first medicament, it would have been apparent to a skilled artisan that one could add additional active agent as needed. Furthermore, it is noted that the step of mixing components in a method of making a pharmaceutical dry powder is conventionally practiced in the art. It is obvious that the order of mixing ingredients in a composition and the relative amount of ingredients in a composition are clearly result specific parameters. The amount of a specific ingredient in a composition and the order of steps in a process are clearly result effective parameters that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed and the optimal order of combining said ingredients to achieve the desired results.

Applicant acknowledges that *Clarke* discloses a pharmaceutical composition comprising formoterol or a fumarate salt thereof and that the pharmaceutical composition is suitable for use in treating inflammatory or obstructive airways diseases. Regardless, *Clarke* does not remedy the deficiencies in *Sarlikiost*. Although *Clarke* discloses mixing the components of its compositions, like *Sarlikiost*, it does not disclose or suggest the specific mixing steps of the present method, the order of the steps, and that different medicaments in different amounts are mixed in a specified order based on their relative amounts. Therefore, the combination of *Sarlikiost* and *Clarke* fails to render the present invention obvious.

Accordingly, withdrawal of the rejection is respectfully requested.

Conclusion

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone Applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: August 28, 2006

Respectfully submitted,

By _____

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